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July 10, 1981

Congressman Charles Rose
Chairman, Subcommittee on Tobacco
and Peanuts
The House of Representatives
Rayburn Building, Room 2435
Washington, D.C. 20515

Dear Congressman Rose:

The following is a summary of my notes on our visit to Dr. James White at UC San Diego, as per our discussion. Unfortunately, despite the statement in the editorial of the New England Journal of Medicine (27 March 1980), Dr. White and his co-author did not "faultlessly demonstrate a reduction in measures of small airways of healthy non-smokers exposed to cigarette smoke in the work place". It is apparent from our visit and the article that there were various fault to the present study, which shall be discussed.

The problems with the research design are as follows:

The participants were not only volunteers, but generally had to pay for the physical fitness course; this is the reason most were white-collar. Employers in specific factories invited White to run the physical fitness course in their factories as well, which would also bias the population sample. Blue-collar workers were not distributed randomly. [It has to be assumed that volunteers in the physical fitness courses fall into unrepresentative categories: the highly motivated, with an interest in health and usually healthier, those who are worried about health and generally less healthy; the first group would include fewer smokers and the second group would include more smokers.]

The questionnaire utilized was not a validated one per se, test - retest comparisons were made only on the smoking questions and very small groups of subjects. The smoking information was not validated. There were no test - retest or valiations on symptoms asked in the questionnaire. The questionnaire itself was derived by the investigator, and included some questions from standard questionnaires; this did not appear to include standard

respiratory questions, and, in fact, various typical respiratory questions (such as phlegm) were not asked. The questionnaire did not include questions on attitude, but did include questions on activity levels and jobs (duration, type). The questionnaire did ask how many smokers were in their work area, room size, and nature of the air conditioning. It also included questions about residences in the last 20 years (zip codes), so that exposures away from work were assessed by residental location. A question was asked about smokers in the home. [Thus, the smoking information is not validated, but is probably relatively accurate. The information about exposure to passive smoking is only approximate, as is the information on other occupational exposures. Exposures to air pollutants or to unknown toxic gases in the working place is only approximate, and their effects underestimated.]

Dr. White presented a paper to the American College of Sports Medicine; the abstract for which in 1977 indicated there were 7,122 subjects enrolled between 1969 and 1977. However, in the New England Journal of Medicine article, he states that the base population analyzed is only 5,210 smokers and non-smokers enrolled between 1969 and 1979. Although he excluded all the ex-smokers, some whose zip codes were missing, his answers as to why the rest of the subjects were excluded were entirely unclear and tend to indicate potential bias in selection of subjects for consideration for analyses. It might be added that the 2,100 subjects analyzed in the NEJM article and those analyzed and presented in the Sports Medicine abstract appear to be the same as they yield exactly the same table of results (as determined from comparison of the table in the Sports Medicine manuscript and the NEJM table).

In addition to the sources of biases mentioned above, it is apparent that the non-smokers in clean work environments and those in smoking work environments have not only chosen not to smoke, but it is likely that those non-smokers working in smoking environments may be different for a variety of reasons from non-smokers working in clean environments. Furthermore, it is apparent that the non-smokers in non-smoking environments are quite different in that their lung function is "super normal" in comparison even with to Seventh Day Adventists (the source of the Morris prediction equations).

Dr. White did state that from the questionnaire and from the baseline tests that there were no significant differences in the three non-smoking/non-inhaling groups in terms of the amount of previous exercise, or oxygen consumption, but he was unsure of the difference in percent of body fat. Smokers did have less body fat, were less in terms of having lower oxygen consumption, and had less activity. He says further that there were no differences between the groups

in terms of childhood respiratory history (lower respiratory tract illnesses) from his submitted quesionnaire information, but he did not ask about family history. He did not ask sufficiently about respiratory questionnaires to appropriately exclude groups on the bases of productive cough ("cough bronchitis"). He states that there were no differences in prevalence rates of questionnaire responses by zip codes; if so, this contradicts other evidence vis-a-vis the effects of air pollution in these areas. He was not able to assess other exposures such as those from hobbies, exposures to gas stoves, or transportation. In terms of passive smoking in the home, he excluded such passive smokers from the non-smoking and passive smoking groups, but not from any smoking groups. He was not able to provide any information about the distribution of characteristics in those eliminated from the original 7,000 or the 2,208 that qualified because of other questionnaire results.

In regards to the pulmonary function testing done by Dr. White, it must be first noted that the instrument used is not considered a satisfactory instrument in that it is non-linear (highly biased) and both high volumes and low volumes. [This has the effect of maximizing differences in that anyone with minor aberrations of total vital capacity or of flows at the end of the flow volume curve would have very different, that is, low, flows.] The comparisons that Dr. White did and reported on in his response letter in the NEJM (14 August 1980) would not in any way modify this opinion. Furthermore, Dr. White was the only pulmonary function technician and reader. Even though he was trained at the VA hospital and his techniques were evaluated by test - retest and by comparison to other readers, any biases inherent in Dr. White's thinking (see below) would effect the way he read the tests. Furthermore, he took the FEV_1 and flows off the same spirogram using an approximation technique published by Morris, et al., which is not adequate or accurate representation of those measures. All of his tests were baseline tests done after two and half hours in the classroom in the evening in those without acute respiratory illnesses (usually on a Monday or Tuesday evening); thus, there is probably little diurnal variation or pretest biases other than those experienced by the workers during their work day and in their activities prior to the classroom. Although it is difficult to judge the effects of these factors, they may have influenced the test results, especially in those with any significant exposures during the day.

The major problem with the pulmonary function test results as reported is that they are not age- and height-adjusted, since lung volumes and flow rates are associated with both of these factors. In other words, Dr. White used raw values of flows and volumes to do comparisons. He did this on the assumption that the mean age and height were similar for the different groups. This is a mistake,

since the distributions for those ages and heights could have differred. Furthermore, his quoted figures for percent predicted are strictly for the average person age 49 with an average height, ane does not represent the group for which they are provided. In terms of these statistical analysis, he just choose the SNK package among many. There are no correlation coefficient per se. "Normality" was not an objective of this study, so he cannot state anything about the normality of the subjects studied, including those he considered to have significantly different results from the non-exposed non-smokers. He does not understand the difference between clinical meaningfulness and statistical significance. It is quite obvious that the majority of those in the passive smoking and in the non-inhaling group are quite normal and that very few would be considered abnormal by any criteria.

In his reported results, he quotes as incorrect significance level of $p<.005$, where as the level provided by the technique is $p<.05$. This is very different, given the number of comparisons made, and indicates that some of the results would not be significant if corrections were made for the number of comparisons. Furthermore, the data presented in Table 1 was used to recompute the SNK analysis by Mary C. Townsend, MPH (Department of Epidemiology, University of Pittsburgh). Those results differ from those published by Dr. White and are provided in the attachment. The most important of the differences is the finding that the passive smokers and light smokers differ for the male $FEV_{75-85\%}$. Thus, the effect of passive smoking on non-smokers is still unconfirmed, despite Dr. White's unfailing conviction that it is confirmed.

Other minor points: In terms of the carbonmonoxide sampling, although it is stated that it was randomized, it was really on only 40 smoking and 40 non-smoking situations chosen by chance but not by random selection. Dr. Froeb, the co-author with Dr. White, is a private practitioner in La Jolla and helped Dr. White in drafting the NEJM manuscript from the manuscript presented at the American College of Sport Medicine. It might be pointed out that San Diego is not strictly low in air pollution concentrations, nor uniformed throughout the area; this may bias some results. Dr. White performed the pulmonary function tests until "reproducible curves were obtained", but they do not necessarily follow the Intermountain, Snowbird, or ATS recommendations.

In reviewing Dr. White's response to the letter to the Editor in the NEJM (14 August 1980), it is quite clear that Dr. White did not satisfactorily answer all the questions raised, many of which are similar to those raised in this letter. It is questionable, from the discussion, whether Dr. White would pursue any further re-analysis

or the data, nor necessarily could it be pursued. It is questionable, given the basic underlying problems in the research design, that re-analysis of the data would be worthwhile. On the other hand, given other results that contradict Dr. White's, including those now in press (such as Comstock et al., Johns Hopkins, presented at the Society for Epidemiological Research in June of 1981), it would be likely that a panel discussion of passive smoking might be valuable. I will be glad to furnish further discussion or help in that matter.

Sincerely,

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MDL/lsp

	Re-computed SNK Test	Original SNK Test
Female FVC	NS PS NI LS MS HS	NS NI LS PS MS HS
Female FEV1	NS NI PS LS MS HS	NS NI LS PS MS HS
Female FEF 75-85%	NS PS NI LS MS HS	NS PS NI LS MS HS
Male FEF 75-85%	NS PS NI LS MS HS	NS NI PS LS MS HS